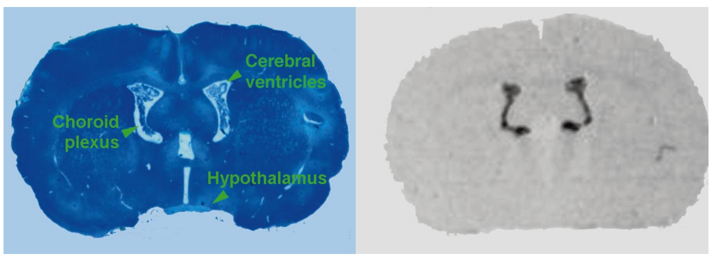
Choroidal Regulations Involved in Altered Gravity

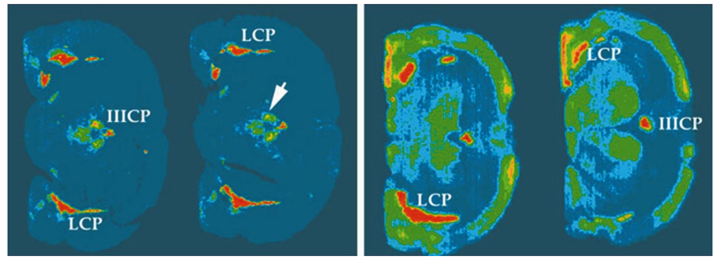
Fundamental Rodent Experiments Supporting Health

Fluid balance and regulation of body fluid production are critical aspects of life and survival on Earth. In space, without gravity exerting its usual downward pulling effect, the fluids of the human body shift in an unnatural, headward direction. After awhile, humans and other mammalian species adapt to the microgravity environment which leads to changes in the regulation and distribution of these body fluids. Previous spaceflight experiments have indicated that production of fluid in the brain and spinal cord, *cerebrospinal fluid (CSF)*, might be reduced in rats exposed to microgravity.



Dr. Gabrion will study the effects of microgravity on proteins responsible for water and ion transport, in the brain and in other tissues. The choroid plexus which produces cerebrospinal fluid (CSF) is located in the cerebral ventricles (left). The right panel illustrates detection of aquaporin 1 messenger RNAs in the choroid plexus (black staining).

In this experiment conducted by Dr. Jacqueline Gabrion (University of Pierre and Marie Curie, France), proteins important for CSF production, and several molecules that regulate water and mineral transport, will be investigated in rats flown on the shuttle. Dr. Gabrion and her team will determine the amounts of these proteins and molecules present in the brain in order to evaluate whether any changes have taken place during the rats' adaptation to microgravity. The levels of different aquaporins (proteins that act as a channel for water transport in and out of cells) will also be investigated in other areas of the brain and body to better understand the regulatory responses affecting these important water channel proteins.



CSF production is influenced by the neurotransmitter serotonin. In frozen brain sections, serotonin receptor messenger RNAs in choroid plexus are shown in red (left). Serotonin receptors have also been detected in choroid plexus through their capability to specifically bind a serotonin-like probe (right, in red).

In addition to producing essential and basic information about fluid production in the brain and body, this research is significant because a reduction in CSF production may contribute to several discomforts (headaches, nasal stuffiness, fullness in the head) frequently endured by astronauts during adaptation to spaceflight. This experiment will reveal fundamental information about the mechanisms involved in cerebral adaptation and fluid balance during spaceflight.

Earth Benefits and Applications

Because of its impact on fluid balance, spaceflight provides unique opportunities to investigate mechanisms of adaptation that involve fluid balance in the brain, kidneys and lungs. This experiment will contribute to a better understanding of basic mechanisms which regulate body fluid balance and homeostasis, and is important for the advancement of fundamental biology.

Principal Investigator: Dr. Jaqueline Gabrion, University of Pierre and Marie Curie, Paris, France
Project Scientist: Marilyn Vasques, NASA Ames Research Center
Project Manager: Rudy Aquilina, NASA Ames Research Center

Choroid regulation background information

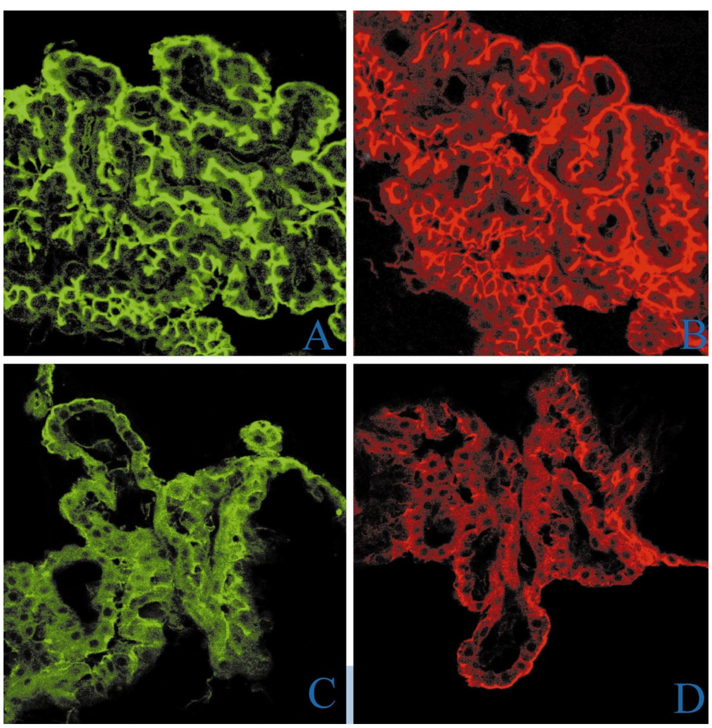
Science

Spaceflight is well known to induce headward fluid shifts and thus offers unique opportunities to analyze the role of gravity in body fluid distribution and fluid balance. However, the difficulties involved in measuring CSF volume and flow in these extreme experimental conditions, have prevented extensive study of CSF production and its transport processes during adaptation to altered gravity. To begin to understand CSF balance during adaptation to altered gravity, Dr. Gabrion and her team initiated studies over 10 years ago to determine the effects of spaceflight on choroidal structures and regulation in the rat.

Science Discipline Supported

This experiment supports NASA's priorities for research aimed at understanding fundamental biological processes in which gravity is known to play a direct role and alleviating problems that may limit astronauts' ability to survive and/or function during prolonged spaceflight.

This STS-107 experiment specifically focuses on 2 important families of transport proteins and on the biochemical signaling molecules that regulate CSF production. Biosynthesis of choroidal *Aquaporin 1* and *sodium-potassium (Na-K) dependent ATPase* will be studied using molecular staining techniques on fixed and/or frozen samples of choroid plexus. The expression levels of different aquaporins will also be investigated in other brain areas, the hypophysis, the kidney, and the lung.

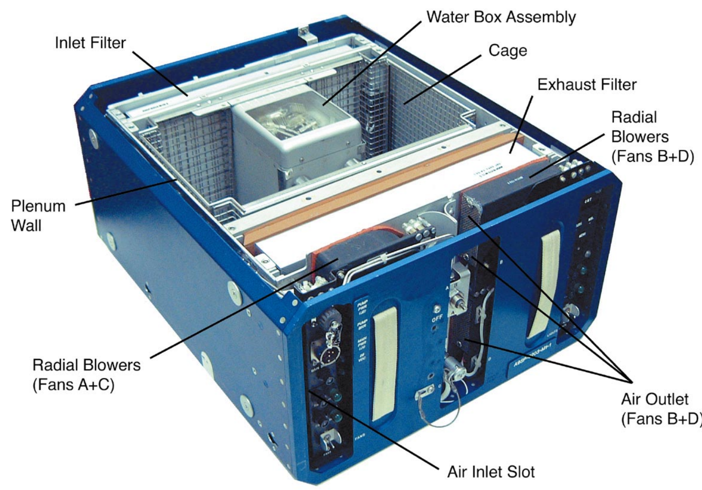


Immunodetection of aquaporin 1 (in green) and sodium-potassium ATPase (in red) at the apical pole of choroid plexus, (A, B) in a control rat and (C,D) in a ground-based model simulating some effects of spaceflight. A net decrease in both proteins was noted at the epithelial cells, suggesting that CSF production was decreased.

Previous flight experiments have demonstrated that reduced gravity dramatically alters the fine structure, functions, and maturation of the choroid plexus in the rat brain. Although no direct measurements of CSF secretion in microgravity have been performed to date, these findings indicate that adult rats likely experience a net reduction in CSF production during spaceflight. Such results might be generalized to humans and could partly explain headaches frequently endured by astronauts in space.

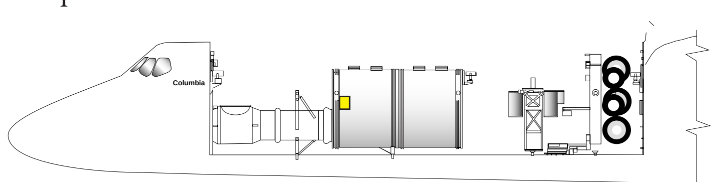
Hardware

The Animal Enclosure Module (AEM) is a rodent habitat that provides ventilation, continuous filtered air flow to control waste and odor, timed lighting, food in the form of foodbars attached to the side of the cage, and a water supply which can be refilled as required. Rodents in the cage compartment of the AEM are not accessible but can be viewed through the clear lexan cover. This also allows for viewing of water level remaining in the AEM water box.



This experiment is part of the FRESH-02 (Fundamental Rodent Experiments Supporting Health) payload which consists of 13 rats housed in 3 Animal Enclosure Modules (AEMs). The animals, which will be shared among several different investigators, will experience microgravity for 16 days on board the shuttle Columbia. The Animal Enclosure Modules have been used successfully on many previous shuttle flights.

The AEM has been designed for minimum crew interaction and the animals adapt very well to this virtually self-contained system. The only nominal operations required are a daily hardware check, a daily visual animal health check, and periodic water refills.



Approximate location of this payload aboard STS-107

Picture credits. Gabrion (pages 1, 2), Ames Research Center (AEM).